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OVERVIEW OF SUBLINGUAL TABLETS

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ABSTRACT

Drug delivery via the oral mucous membrane is considered to be a promising alternative to the oral route. Sublingual route is a useful when rapid onset of action is desired with better patient compliance than orally ingested tablets. In terms of permeability, the sublingual area of the oral cavity (i.e. the floor of the mouth) is more permeable than the buccal (cheek) area, which in turn is more permeable than the palatal (roof of the mouth) area. The portion of drug absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes giving acceptable bioavailability. Various techniques can be used to formulate sublingual tablets. New sublingual technologies address many pharmaceutical and patient needs, ranging from enhanced life-cycle management to convenient dosing for paediatric, geriatric, and psychiatric patients with dysphagia. This review highlights the different sublingual dosage forms, factors affecting the sublingual absorption, advantages, various *in vitro* and *in vivo* evaluation parameters and commercially available sublingual dosage forms[1]..

Keywords: Sublingual delivery, Oral cavity, Dysphagia, Improved bioavailability.

INTRODUCTION

The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic Processes. A fast dissolving tablet system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in form of liquid. Recently fast dissolving formulation is popular as NDDS because they are easy to administer and lead to better patient compliance. Paediatric and geriatric patient have difficulty in swallowing the conventional dosage forms these dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity. The medication can then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract[2, 3, 4] . The oral route of administration is considered as the most

widely accepted route. The unique environment of the oral cavity offers its potential as a site for drug delivery. Because rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver. The continuous secretion of saliva results in rapid removal of released drug and this may desire that the oral cavity be restricted to the delivery of drugs, which have a short systemic circulation. The mucin film, which exists on the surface of the oral mucosa provide an opportunity to retain a drug delivery system in contact with the mucosa for prolonged periods if it is designed to be mucoadhesive. Such system ensures a close contact with absorbing membrane, thus optimizing the drug concentration gradient across the biological membrane and reducing the differential pathway. The oral mucosa may be potential site for controlled or sustained drug delivery. Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenterals are painful drug delivery, so most patient incompliance[5].Sublingual administration of the drug means placement of the drug under the tongue and drug reaches directly into the blood stream through ventral surface of the tongue and floor of the mouth. The drug solutes are rapidly absorbed into the reticulated vein which lies underneath the oral mucosa, and transported through the facial veins, internal jugular vein, and braciocephalic vein and then drained in to systemic circulation[1] The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes[6,7,8]. Sublingual products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia[9].)

How it is beneficial for patients

- Ø Ease of administration to patients who refuse to swallow a tablet, such as paediatric, geriatric patients and psychiatric patients.

- Ø Convenience in administration of drug and accurate dosing as compared to liquid formulations.
- Ø Water is not required for swallowing the dosage form, which is convenient feature for patients who are travelling and do not have immediate access to water.
- Ø Good mouth feels property helps to change the basic view of medication as "bitter pill", particularly for paediatric patients.
- Ø Fast dissolution of medicament and absorption which will leads to rapid, onset of action.
- Ø Some drugs are absorbed from the mouth pharynx and esophageus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Ø It provides advantages of liquid formulations in the form of solid dosage form.
- Ø Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Advantages [10]

- A relatively rapid onset of action can be achieved compared to the oral route, and the formulation can be removed if therapy is required to be discontinued.
- Liver is bypassed and also drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract
- Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.
- Low dosage gives high efficacy as hepatic first pass metabolism is avoided and also reduces the risk of side effects.
- The large contact surface of the oral cavity contributes to rapid and extensive drug absorption.
- Due to rapidity in action these sublingual dosage forms are widely used in emergency conditions e.g. asthma.
- Rapid absorption and higher blood levels due to high vascularisation of the region and therefore particularly useful for administration of antianginal drugs.

- They also present the advantage of providing fast dissolution or disintegration in the oral cavity, without the need for water or chewing.

Disadvantages[10]

- Ø Since sublingual administration of drugs interferes with eating, drinking, and talking, this route is generally considered unsuitable for prolonged administration.
- Ø Although this site is not well suited to sustained-delivery systems.
- Ø Sublingual medication cannot be used when a patient is uncooperative or unconscious.
- Ø The patient should not smoke while taking sublingual medication, because smoking causes vasoconstriction of the blood vessels. This will decrease the absorption of the medication.

Criteria of selection of drug for Sublingual Tablets formulation

The ideal characteristics of a drug for in vivo dissolution from an Sublingual Tablets include

- Dose lower than 5 mg about 1.25 mg,2.5 mg,0.25 mg.
- Molecular weight <500 da.
- Good stability in water and saliva
- Lipophilic in nature, unionized at the sublingual cavities pH
- Ability to diffuse and partition into the epithelium of the upper GIT (log P>1, or preferably>2)
- Lower water solubility
- Passive diffusion drug absorption
- Bcs-class 2 and 1.
- Drug which have higher eliminated half life and employ against immediate action required disease.
- Drugs which have dosing frequency are higher.

SUBLINGUAL GLANDS[11]

The three major salivary glands are the parotid, submandibular and sublingual. There are numerous sub mucosal glands scattered throughout the non-keratinizing mucosa of the oral cavity.The three large glands have some common macroscopic and microscopic features.

Macroscopic Appearance

All the glands have a pinkish-brown hue.

Microscopic Appearance

The salivary glands have a tubulo-acinar structure with a bilayered cuboidal epithelium. The outer layer consists of mucous or serous cells. The basement layer contains myoepithelial cells which can constrict the acini and tubules to move saliva. The ducts are initially lined by similar epithelium, which gradually becomes columnar as ducts merge into larger structures.

Parotid gland

Structure

The parotid gland is the largest salivary gland of the body. It is located in the postero-lateral face, extending from the superficial skin to the carotid sheath deep to the mandible. It lies between the mastoid process posteriorly and the ramus of the mandible interiorly. It extends over the surface of sternocleidomastoid posteriorly and the masseter muscle interiorly. The parotid duct passes superficial to masseter, turns deeply at its anterior border and empties into the inner wall of the cheek opposite the third molar tooth.

Contents

The parotid gland contains nerves, vessels and lymph nodes which pass through it or lie within its substance.

Arterial Structures

The external carotid artery is deepest, initially outside the gland becomes enveloped as it ascends. The posterior auricular, maxillary and superficial temporal arteries arise within the gland.

Venous Structures

combines with the posterior auricular vein to form the external jugular) and a posterior division was combines with the common facial vein to empty into the internal jugular.

Neural Structures

The facial nerve emerges from the styloid foramen just posterior to the parotid gland. It curves an interiorly after giving off the posterior auricular branch to enter the posterior surface of the gland. It then divides into temporal, zygomatic, buccal, mandibular and

cervical branches that supply the muscles of facial expression. The facial nerve and its branches form an important landmark, dividing the parotid into superficial and deep lobes. The deep lobe is relatively inaccessible due to significant side effects arising from sacrifice of the nerves.

Lymph Nodes

Parotid lymph nodes lie in the most superficial part of the parotid. They drain lymph from the lateral forehead and the lateral orbital structures.

Relations

It is superficially related to the skin. Posteriorly, related to the sternocleidomastoid and mastoid process. Inferiorly, related with the carotid sheath (internal carotid, internal jugular, cranial nerves IX-XII), the digastrics muscle, styloid process and medial pterygoid. Anteriorly, related to the parotid duct and masseter. Superiorly, related to the zygomatic arch.

Neurovascular Supply

Arterial Supply

The parotid gland is supplied by small branches from the external carotid artery and its named branches.

Venous Drainage

Veins drain to the retromandibular vein and its tributaries.

Lymphatics

The parotid contains superficial lymph nodes in its superior lobe. These nodes drain deeply to the deep cervical nodes or superficially to the superficial cervical nodes.

Innervation

The skin of the parotid is supplied by the great auricular nerve (ascending from C_2 and C_3 branches) and the auriculotemporal branch of the maxillary nerve (V_2). Secret-motor supply to the parotid is derived from the glosso-pharyngeal nerve (IX), via the tympanic branch, tympanic plexus, lesser petrosal nerve and the pterygopalatine ganglion.

Submandibular glands

Structure

The Submandibular glands lie on the internal surface of the mandible, divided into two parts by the posterior edge of mylohyoid. The superficial part lies on the inferior side of

mylohyoid and is significantly larger. The deep part lies on the superior/internal side of mylohyoid and gives off the submandibular duct. The submandibular duct passes anteriorly and medially to end in the sublingual papilla near the midline, adjacent to the lingual frenulum. Submandibular lymph nodes are located near the mandibular part of the gland.

Relations

The submandibular gland is internal to the mandible and inferior to the floor of the mouth. The mandible is posterior.

Neurovascular Supply

Arterial Supply

Arterial supply to the submandibular gland is derived from facial and lingual arteries.

Venous Drainage

Blood is returned via lingual and facial veins.

Lymphatics

The submandibular nodes lie in close proximity to the gland, or within its structure. Lymph flows from this region to the upper deep cervical nodes (level II).

Innervations

The **submandibular ganglion** is the source of neural supply to the submandibular gland. This small ganglion is associated with the lingual nerve as it passes anteriorly along the floor the mouth. Parasympathetic fibers arrive via the chord tympani, a branch of the facial nerve VII. Sympathetic fibers are derived from the facial artery plexus. General sensory nerves arrive from the lingual nerve (V_3).

Sublingual gland

Structure

The sublingual gland is the smallest of the named salivary glands. It lies in the floor of the mouth near the midline, covered by mucosa and lying on the mylohyoid. The mandible is lateral and the genioglossus is medial. Unlike the other major salivary glands, the sublingual gland has numerous small ducts which empty either into the floor of the mouth or into the submandibular duct.

Neurovascular Supply

Arterial Supply

The sublingual branch of the lingual artery and submental branch of the facial artery contribute to the supply of the sublingual gland.

Venous Drainage

Either accompanying sublingual veins to the common facial vein or passing laterally to the facial vein.

Lymphatics

The sublingual gland drains primarily to sub-mental nodes.

Innervation

Innervation is via the submandibular ganglion, described with the submandibular salivary gland. Nerves passing to the sublingual gland leave the ganglion and region the lingual nerve, before departing again to supply their target organ.

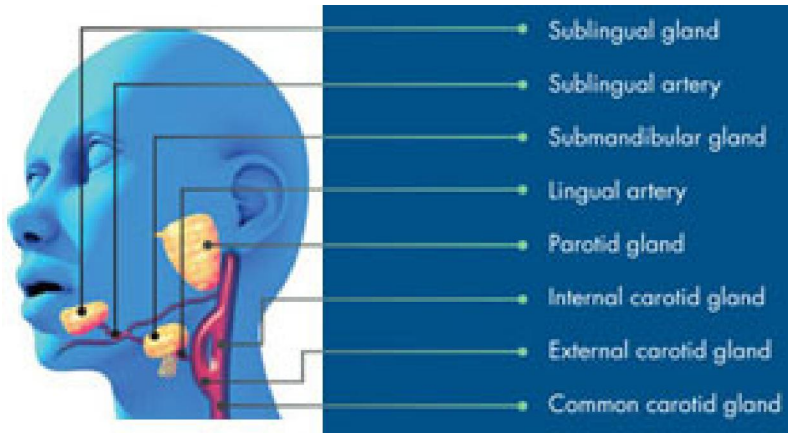

Figure 1: connection sublingual gland and sublingual artery

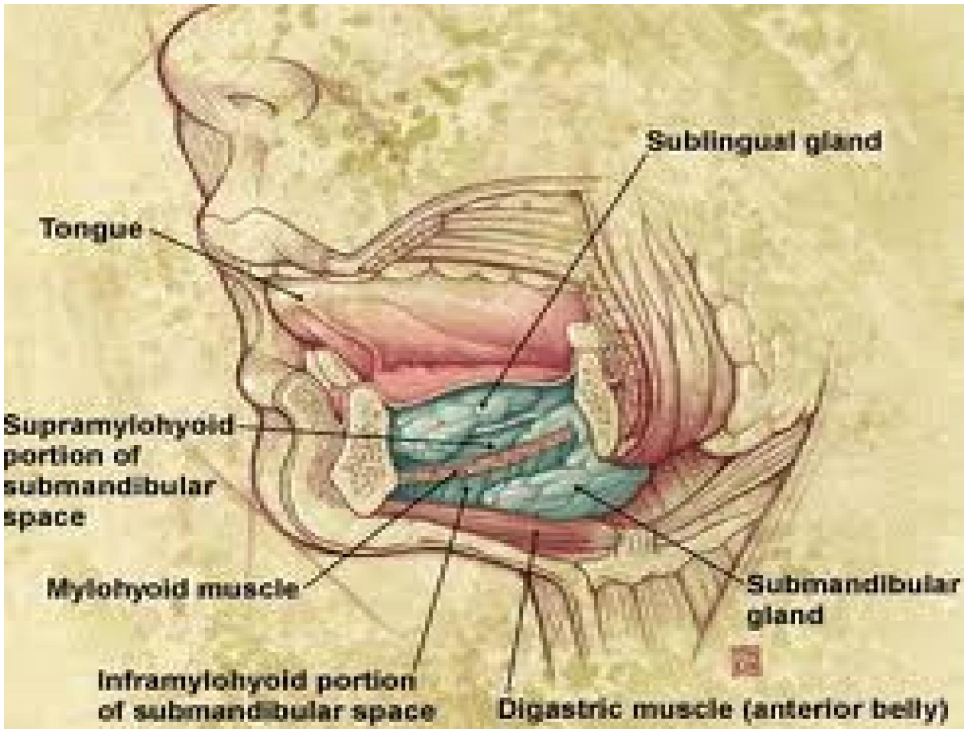

Figure 2: sublingual glands

The Mechanism of Sublingual Absorption

The absorption potential of the buccal mucosa is influenced by the lipid solubility and therefore the permeability of the solution (osmosis), the ionization (pH), and the molecular weight of the substances. For example, absorption of some drugs via the buccal mucosa is shown to increase when carrier pH is lowering (more acidic) and decrease with a lowering of pH (more alkaline). The cells of the oral epithelium and epidermis are also capable of absorbing by endocytosis (the uptake of particles by a cell as if by hollowly wrapping itself around it. These engulfed particles are usually too large to diffuse through its wall). It is unlikely that this mechanism is used across the entire stratified epithelium. It is also unlikely that active transport processes operate within the oral mucosa. However, it is believed that acidic stimulation and uptake into the circulatory system. The mouth is lined with a mucous membrane which is covered with squamous epithelium and contains mucous glands. The buccal mucosa is similar to the sublingual mucosal tissue. The salivary glands consist of lobules of cells which secrete saliva through the salivary ducts into the mouth. The three pairs of salivary glands are the

Parotid, the Sub mandibular and the Sublingual which lies on the floor of the mouth. More acid the taste the greater the stimulation of salivary output, serving also to avoid potential harm to acid sensitive tooth enamel by bathing the mouth in copious neutralizing fluid. With stimulation of salivary secretion oxygen is consumed and order to keep the tablet in place. Swallowing of saliva should also be avoided since the saliva may contain dissolved drug. Bland excipients are used to avoid salivary stimulation. Vasodilator substances are produced, and the glandular blood flow increases, due to increased glandular metabolism. The sublingual artery travels forward to the sublingual gland, it supplies the gland and branches to the neighboring muscles and to the mucous membranes of the mouth, tongue and gums. Two symmetrical branches travel behind the jaw bone under the tongue to meet and join at its tip. Another branches meets and anastomoses with the submental branches of the facial artery. The sublingual artery system stems from the lingual artery – the body's main blood supply to the tongue and the floor of the mouth – which arises from the external carotid artery. The proximity with the internal carotid artery allows fast access to its route supplying the greater part of the cerebral hemisphere[19].

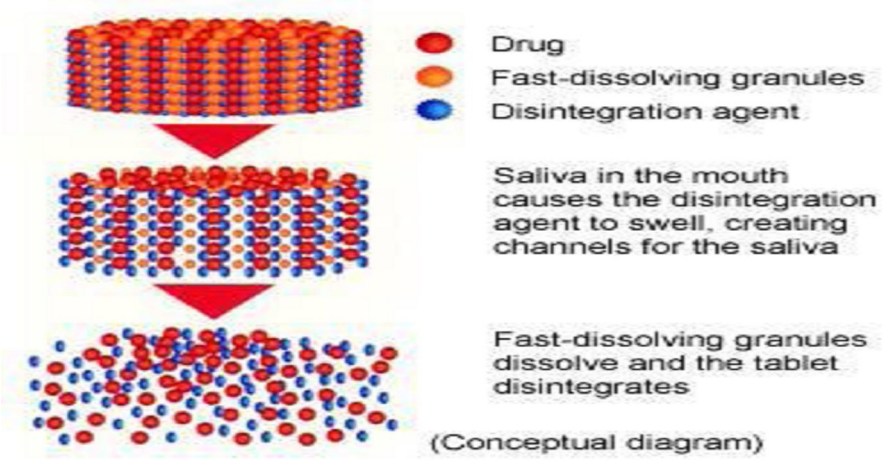

Figure 3: drug disintegration in saliva

Factors affecting the sublingual absorption[10]

Ø **Lipophilicity of drug**: For a drug to be absorbed completely through sublingual route, the drug must have slightly higher lipid solubility than that required for GI absorption is necessary for Passive permeation.

- **Solubility in salivary secretion**: In addition to high lipid solubility, the drug should be soluble in aqueous buccal fluids i.e. biphasic solubility of drug is necessary for absorption.
- **pH and pKa of the saliva:** As the mean pH of the saliva is 6.0, this pH favours the absorption of drugs which remain unionized. Also, the absorption of the drugs through the oral mucosa occurs if the pKa is greater than 2 for an acid and less than 10 for a base.
- **Binding to oral mucosa**: Systemic availability of drugs that bind to oral mucosa is poor.
- **Thickness of oral epithelium**: As the thickness of sublingual epithelium is 100-200 µm which is less as compared to buccal thickness. So the absorption of drugs is faster due to thinner epithelium and also the immersion of drug in smaller volume of saliva.
- **Oil to water partition coefficient:** Compounds with favourable oil to-water partition coefficients are readily absorbed through the oral mucosa. An oil-water partition coefficient range of 40-2000 is considered optimal for the drugs to be absorbed sublingually.

SUBLINGUAL FORMULATION

Sublingual tablets

They are to be placed under the tongue and produce immediate systemic effect by enabling the drug absorbed directly through mucosal lining of the mouth beneath the tongue. The drug absorbed from stomach goes to mesenteric circulation which connects to stomach via portal vein. Thus absorption through oral cavity avoids first pass metabolism. The tablets are usually small and flat, compressed lightly to keep them soft. The tablet must dissolve quickly allowing the API to be absorbed quickly. It is designed to dissolve in small quantity of saliva. After the tablet is placed in the mouth below the tongue, the patient should avoid eating, drinking, smoking and possibly talking in order to keep the tablet in place. Swallowing of saliva should also be avoided since the saliva may contain dissolved drug. Bland excipients are used to avoid salivary stimulation[12,13].

Fast disintegrating sublingual tablets (FDT)

FDT is defined as a solid dosage form that contains medicinal substances and disintegrates rapidly (within few seconds) without water when kept on the tongue. The

drug is released, dissolved, or dispersed in the saliva, and then swallowed and absorbed across the GIT [(14).] FDTs also are also called as Orodispersible tablet, mouth-dissolving, quick-dissolving, fast-melt, and freeze-dried wafers. Tablets that disintegrate or dissolve rapidly in the patient's mouth are convenient for young children, the elderly and patients with swallowing difficulties and in situations where potable liquids are not available. Direct compression is one of the techniques which require the incorporation of a superdisintegrant into the formulation, or the use of highly water soluble excipients to achieve fast tablet disintegration. Compared to conventional dosage form the drug dissolution, its absorption as well as onset of clinical action and its bioavailability may be significantly greater [15,16,17.]

Though chewable tablets are available in the market, they are not same as the new FDTs. Patients for whom chewing is difficult or painful can use these FDTs. It can be used easily in infants and in children who have lost their primary teeth hand who do not have full use of their permanent[18].

Bioadhesive sublingual tablets[19]

The new sublingual tablet concept presented is based on interactive mixtures consisting of a water soluble carrier covered with fine drug particles and a bioadhesive component. With this approach, it is possible to maintain rapid dissolution in combination with bioadhesive retention of the drug in the oral cavity. Bio adhesion is usually defined as the bond formed between two biological surfaces or between a biological and a synthetic surface. Problem associated with sublingual tablet formulation is that there is always a risk that the patient will swallow part of the dose before the active substance has been released and absorbed locally into systemic circulation. This could results an unwanted prolongation of the pharmacological effect. Addition of a bio adhesive component is a well-known method of increasing the possibility of a more site-specific release. However, this concept is normally applied to non-disintegrating tablets or disc to achieve extended release of the active substance and, consequently, such a system will not be suitable for a fast acting formulation. Therefore, it would be of interest to study a disintegrating tablet which releases the drug quickly, but which also has bioadhesive properties which could prevent the drug from being swallowed.

Lipid matrix sublingual tablets[19]

Such tablets are formulated using advances in sublingual and liposomal technology to create a Dosage form that offers a faster and more complete absorption than traditional oral routes of administration. The lipid matrix sublingual tablet is a bio available, quick, convenient and consistent dosage form for many neutraceuticals that are often taken orally. For e.g., Glutathione MB12 (methylcobalamin) melatonin.

Sublingual vitamin tablet[19]

Vitamin D i.e. cholecalciferol is a natural precursor of calcium regulating hormone calcitriol. Vitamin D is thus used in hypocalcaemia/ hyperparathyroidism. Because of its incomplete absorption from GI tract, local intestinal degradation and hepatic metabolism, it is given sublingually**.**

Superdisintegrants use in FDT sublingual tablets. As Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. But have one drawback that it is hygroscopic therefore not used with moisture sensitive drugs. And this superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

TABLE 1: LIST OF SUPERDISINTEGRANTS [20]

EXAMPLE	SUPER-DISINTEGRANTS	MECHANISM OF ACTION	SPECIAL COMMENT
Crosslinked cellulose	Crosscarmellose® Ac-Di-Sol® Primellose® Vivasol®	Swells 4-8 folds in < 10 seconds. Swelling and wicking both.	Swelling is in two dimensions. -Direct compression or granulation-Starch free
Crosslinked PVP	Crosspovidone	Swells 7-12 folds in <30 seconds	Swells in three dimensions and high level serve as sustain release matrix
Crosslinked starch	Sodium starch glycolate	Swells 7-12 folds in <30 seconds	Swells in three dimensions and high level serve as sustain release matrix
Cross linked alginic acid	Alginic acid NF	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Natural super Disintegrates	Soya polysaccharides	Rapid Dissolving	Does not contain any starch or sugar. Used in nutritional products.

SELECTION OF SUPER-DISINTEGRATES.

The ideal superdisintegrant should have [20]:

- Poor solubility.
- Poor gel formation.
- Good hydration capacity.
- Good moulding and flow properties
- No tendency to form complexes with the drugs.
- Good mouth feel.
- It should also be compatible with the other excipients and have desirable tableting properties.

MECHANISM OF ACTION OF DISINTEGRATES.

a. Swelling[21]

General mechanism of action for tablet disintegration is Swelling tablets through high porosity expression poor Disintegration due to lack of sufficient swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing Fraction is very high; fluid is unable to penetrate in the tablet and disintegration is again slows down.

b. Porosity capillary action (wicking) [21]

While we place the drug into appropriate aqueous medium, the Medium enters into the tablet and replaces the air absorbed on the particles, which softness the intermolecular bond and Breakdowns the tablet into fine particles. Water uptake by Tablet depends upon hydrophilicity of the drug/excipient and on tableting environments. For these types of disintegrates, Maintenance of porous structure and low interfacial tension towards aqueous fluid is essential which helps in Disintegration by manufacture a hydrophilic system around the Particles.

c. Heat of wetting (air expansion) [21]

When disintegrates through exothermic properties gets wetted, Localized stress is produced due to capillary air expansion, this helps in breakdown of tablet.

d. Due to release of gases[21]

Carbon dioxide released within tablets continuously wetting Due to contact between bicarbonate and carbonate with citric Acid or tartaric acid. The tablet disintegrates due to generation of pressure inside the tablet. As these disintegrates are highly Sensitive to small changes in humidity level and temperature, Strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added Immediately prior to compression or can be added in to Separate fraction of formulation.

e. By enzymatic reaction[21]

These enzymes destroy the binding action of binder and helps In disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous Increase in the volume of granules to promote disintegration.

f. Due to disintegrating particle repulsive forces[21]

(Secondary to wicking)

The swelling of tablet made through 'non-swellable' Disintegrates. Guyot-Hermann has planned particle repulsion Theory based on the observation that non-swelling particle also Cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and Water is required for it.

g. Due to deformation[21]

During the tablet compression, disintegrated particles become deformed and these deformed particles get into their normal Structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch remained Improved when granules where extensively deformed during Compression.

EVALUATION TEST OF SUBLINGUAL TABLETS

- **Hardness and thickness**

The test is done as per the standard methods. The hardness of three randomly selected tablets from each formulation is determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale is noted down [23].The thickness of three randomly selected tablets from each formulation is determined in mm using a vernier caliper (Pico India). The average values are calculated [22].

- **Drug Content**

Randomly ten tablets are selected from formulation, finely powdered and powder equivalent mg of drug is accurately weighed and transferred to 100 ml volumetric flasks containing solution of desired pH. The flask is shaken to mix the contents thoroughly. The volume is made up to the mark with solution and filtered. One ml of the filtrate is suitably diluted and drug content is estimated using a double beam UV-visible spectrophotometer. This procedure is repeated thrice and the average value is calculated [19].

- **Wetting time (WT)**

It is useful for quality control and provides supportive evaluation of these sublingual tablets. Unlike the disintegration test, the wetting test uses minimal water, which may be more representative of the quantity of moisture available sublingually. Using this test, the time required for moisture to penetrate the tablet completely is measured and possibly represents the time required to release drug in the presence of minute volumes of saliva the tablet was placed above absorbent paper fitted into a petri dish. After the paper is thoroughly wetted with distilled water, excess water is completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet is then recorded using a stopwatch [22].

- **Disintegration test**

A relatively simple method with rigorous conditions is developed. Each individual tablet is dropped into 10-ml glass test tube (1.5-cm diameter) containing 2ml distilled water, and the Time required for complete tablet disintegration is observed visually and recorded using a stopwatch. The visual inspection is enhanced by gently rotating the test tube at a 450 angle, without agitation, to distribute any tablet particles that might mask any remaining undisintegrated portion. Sublingual tablets, the disintegration apparatus for oral tablets are used without the covering plastic disks and 2 minutes is specified as the acceptable time limit for tablet disintegration[23].

- **Water absorption ratio**

A piece of tissue paper folded twice is placed in a small Petri dish Containing 6 ml of water. A tablet is put on the tissue paper and allowed to completely wet. The wetted

tablet is then weighted. Water absorption ratio, R was determined using following equation [22].

$$R = 100 \times (W_a - W_b)/W_a$$

where,

R = Water absorption ratio

W_a = Weight of tablet after water absorption

W_b = Weight of tablet before water absorption.

In vitro disintegrating test[22].

Disintegration times for sublingual tablets are determined using USP tablet disintegration apparatus with desired medium. The volume of medium was 900 ml and temp was 37± 2°C. The time in seconds taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus is measured.

In vitro dissolution test [24]

In-vitro release rate of sublingual tablets will be carried out using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus (Paddle method). An aliquot sample of the solution is withdrawn from the dissolution apparatus. The samples are replaced with fresh dissolution medium of same quantity. The samples are filtered through Whatman filter paper No 40 and analyzed in UV spectrophotometer. The percentage drug release is calculated using an equation obtained from the calibration curve.

TABLE 2: MARKETED PRODUCTS OF SUBLINGUAL TABLETS

Brand Name	Category	Strength
Abstral Fentanyl Citrate	Opioid Analgesic	50, 100, 200, 300, 400, 600, 800 µg
Subutex Buprenorphine	Opioid Analgesic	2 and 8mg
Avitan Lorazepam	Antianxiety	1, 2 mg
Edular Zolpidem tartrate	Sedatives/ Hypnotics	5, 10 mg
Isordil Isosorbide dinitrate	Vasodilators	2.5, 5 10mg
Suboxone Buprenorphine HCl	Narcotic + Opioid antagonist	2/0.5, 8/2 mg

CONCLUSIONS

Recently many drugs have been formulated for sublingual drug delivery with an objective of rapid drug release and restricting the region of drug release to mouth. Compared to commonly used tablets, capsules and other oral dosage forms, sublingual absorption is generally much faster and more efficient. Sublingual dosages are convenient for young children, the elderly and patients with swallowing difficulties, and in situations where potable liquids are not available. Peak blood levels of most products administered sublingually are achieved within 10-15 minutes, which is generally much faster than when those same drugs are ingested orally. Sublingual absorption is efficient. The percent of each dose absorbed is generally higher than that achieved by means of oral ingestion. Drug is directly entered to systemic circulation, improve bio availability and produce immediate onset of action.

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